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DOI:

[10.1161/CIRCRESAHA.120.316748](https://doi.org/10.1161/CIRCRESAHA.120.316748)

Document Version

Publisher's PDF, also known as Version of record

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Citation for published version (APA):

Floyd, C. N., Shahed, F., Ukah, F., McNeill, K., O'Gallagher, K., Mills, C. E., Evangelopoulos, D., Lim, S., Mudway, I., Barratt, B., Walton, H., & Webb, A. J. (2020). Acute Blood Pressure-Lowering Effects of Nitrogen Dioxide Exposure from Domestic Gas Cooking via Elevation of Plasma Nitrite Concentration in Healthy Individuals. *Circulation Research*, 127(6), 847-848. <https://doi.org/10.1161/CIRCRESAHA.120.316748>

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Acute Blood Pressure-Lowering Effects of Nitrogen Dioxide Exposure From Domestic Gas Cooking Via Elevation of Plasma Nitrite Concentration in Healthy Individuals

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Air pollution is a major cause of cardiovascular and all-cause mortality. Disentangling the relative contributions of pollutants is challenging, as epidemiological data measuring exposure to one (eg, nitrogen dioxide [NO₂]) is inevitably confounded by exposure to others (eg, particulate matter). Animal studies suggest that inhaled NO₂ has the potential to increase plasma [nitrite]¹; a chemical originally considered to be physiologically inert before we found that its reduction to nitric oxide protects the myocardium against ischemia-reperfusion injury and lowers blood pressure in humans.²

We conducted an acute, randomized, controlled, crossover study to assess the impact of 90 minutes exposure to NO₂ (from sitting next to a domestic gas cooker with gas hobs lit and uncovered) versus control (room air) on plasma [nitrite] (primary end point) and blood pressure (secondary end points) in 12 healthy participants. All underwent both interventions/visits (interval 7–108 days) in a computer-generated randomized order. Baseline characteristics (mean±SD): 26±4 years, 10/12 female, body mass index 21.9±3.0 kg/m², systolic blood pressure 113.8±7.9 mmHg, diastolic blood pressure 72.8±5.7 mmHg. The exposure phase was followed by a 90 minutes washout phase at background [NO₂]. Participants fasted for 12 hours before each visit and received 250 mL low-nitrate water at time 0 h/1.5 h. The study was powered for a difference in plasma [nitrite] of 27±40 nmol/L on repeated-measures, 2-way ANOVA

(α , 0.05 and β , 0.2) following D'Agostino-Pearson normality confirmation, with Sidak post-test (GraphPad Prism v8.2.1).³

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Relative to control, exposure increased ambient [NO₂]: 276.3±38.5 versus 27.6±2.8 ppb ($P<0.001$). Plasma [nitrite] was increased through both the 90 minutes NO₂ exposure and 90 minutes washout ($P<0.001$; Figure [A]). NO₂ exposure decreased both systolic blood pressure and diastolic blood pressure (both $P<0.001$; Figure [B] and [C]). The largest decrease in systolic blood pressure relative to control occurred at 45 minutes (4.6 mmHg [95% CI, 0.2–8.9]; $P=0.032$) and 90 minutes (5.5 mmHg [95% CI, 1.2–9.9]; $P=0.005$). The effect of NO₂ on diastolic blood pressure was maximal at 45 minutes (5.7 mmHg [95% CI, 0.9–10.5]; $P=0.009$).

The temporal relationship between the increase in plasma [nitrite] and systolic blood pressure/diastolic blood pressure reduction (≈ 5 mmHg) is consistent with studies investigating dietary nitrate.² Furthermore, whilst the level of NO₂ exposure (276.3±38.5 ppb) was ≈ 2.5 -fold greater than recommended limits for exposure (eg, World Health Organization guideline 105 ppb 1-hour mean), it is less than that recorded adjacent to busy roads or in some domestic kitchens (≈ 2000 ppb).

Key Words: air pollution ■ blood pressure ■ nitrite ■ nitrogen dioxide ■ particulate matter

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For Sources of Funding and Disclosures, see page 848.

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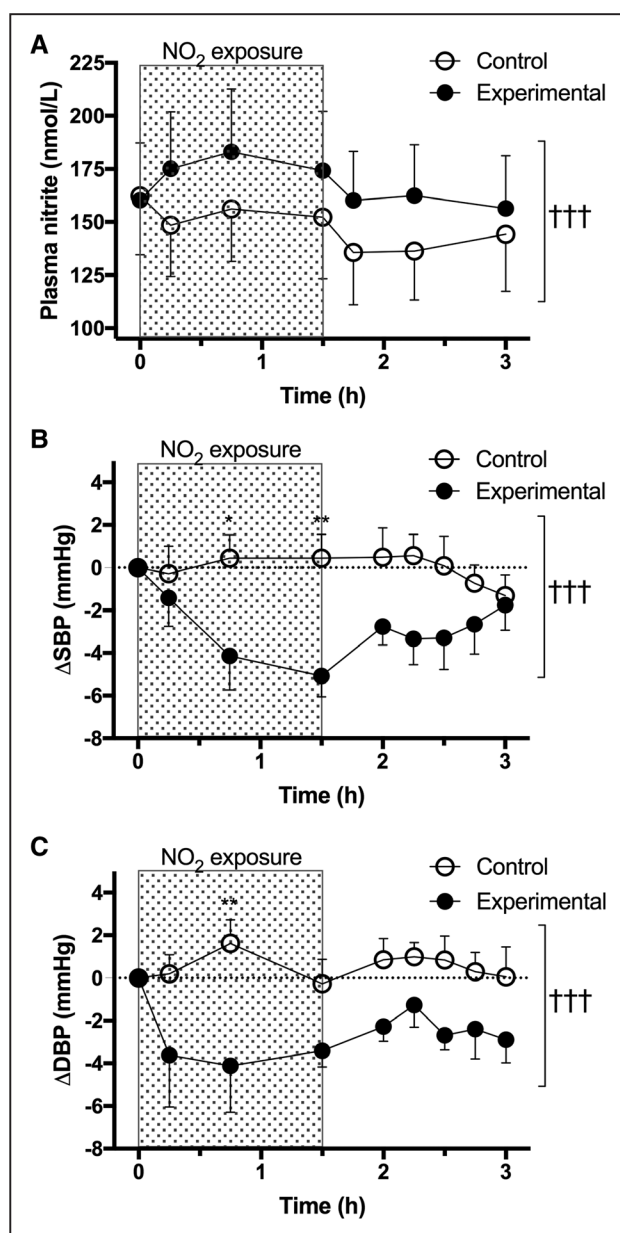


Figure. Effect of nitrogen dioxide (NO₂) exposure on plasma [nitrite] and blood pressure.

Plasma [nitrite] (A), systolic blood pressure (ΔSBP; B), diastolic blood pressure (ΔDBP; C). Comparison between experimental and control shown as *** $P < 0.001$ and individual timepoints as * $P < 0.05$ and ** $P < 0.01$. Data expressed as mean \pm SEM ($n = 12$).

Our model is, therefore, conservative relative to real-world exposure.

Previously, an increase in plasma [nitrite] at 2 hours following diesel exhaust inhalation was thought to be due to particulate matter-mediated induction of inflammatory pathways.³

However, our data suggest a more rapid increase in plasma [nitrite] which favors chemical conversion from NO₂ (eg, via a nitrous acid intermediary) and presents a plausible mechanism through which inhaled NO₂ increases plasma [nitrite].¹ This novel ecophysiological

NO_x cycle may directly feed into the established nitrate-nitrite-nitric oxide pathway and contribute nitric oxide-mediated cardiovascular effects.² Adverse respiratory effects of inhaled NO₂ were not investigated here.¹

These data must be considered in the context of the strong epidemiological association between NO₂ exposure and cardiovascular mortality.¹ However, particulate matter-free NO₂ does not appear to impair either vascular function, fibrinolysis, or affect heart rate variability in patients with coronary heart disease: parameters adversely affected by increased ambient NO₂ exposure in epidemiological studies.^{4,5} This study expands our understanding of how inhaled NO₂ might impact the cardiovascular system, and the role of diet in disease: it is not just what you eat, but how you cook it that matters.

ARTICLE INFORMATION

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Sources of Funding

King's Together Multi and Interdisciplinary Research Scheme (Wellcome Trust Institutional Strategic Support Fund [204823/Z/16/Z]). H. Walton and D. Evangelopoulos's posts part-funded by NIHR-HPRU on Health Impacts of Environmental Hazards at KCL in Partnership with PHE and ICL, London, UK. Internal infrastructure financial support: KCL-BHF Centre, NIHR-CRF/NIHR-BRC at GSTFT/KCL. Views expressed are authors' (not necessarily NHS/NIHR/DHSC/PHE).

Disclosures

None.

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